

Appln No.: 08/822,186

Amendment dated November 3, 2003

In Response to Examiner's Office Action dated July 1, 2003

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks begin on page 12 of this paper.

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AMENDMENTS TO THE CLAIMS

Please amend claims 1, 17, 20-24, 31, 32 and 35.

This listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims:

Claim 1 (currently amended): A device for inducing local bone or cartilage formation, comprising:

~~a purified an osteogenic protein capable of inducing repair of endochondral bone, or cartilage, chondral, or osteochondral defects, said purified osteogenic protein being isolated from naturally occurring sources or produced by recombinant DNA techniques;~~

~~a non-synthetic, non-polymeric matrix selected from the group consisting of collagen, apatites, hydroxyapatites, tricalcium phosphate, and admixtures thereof; and~~

~~a binding agent selected from the group consisting of mannitol, dextran, cellulose, white petrolatum, and salts derivatives thereof;~~

wherein ~~the device does not comprise a synthetic polymer matrix or a demineralized bone matrix, and said~~ binding agent has a viscosity of about 10-200 cP or and a degree of substitution of 0.65-0.90.

Claim 2 (previously presented): The device of claim 1, wherein said osteogenic protein is selected from the group consisting of: OP1, OP2, OP3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP9, BMP10, BMP11, BMP12, BMP15, BMP16, DPP, Vgl, 60A protein, GDF-1, GDF3, GDF5, GDF6, GDF7, GDF8, GDF9, GDF10, GDF11, and variants thereof having conservative amino acid substitutions and substantially similar osteogenic activity.

Claim 3 (previously presented): The device of claim 1, wherein said osteogenic protein is selected from the group consisting of OP1, OP2, BMP2, BMP4, BMP5, BMP6, and variants thereof having conservative amino acid substitutions and substantially similar osteogenic activity.

Claim 4 (previously presented): The device of claim 1, wherein said osteogenic protein comprises an amino acid sequence having at least 70% homology with the C-terminal 102-106 amino acids, including the conserved seven cysteine domain, of human OP1, said osteogenic protein capable of

inducing repair of endochondral bone when implanted together with a matrix in a mammal.

Claim 5 (original): The device of claim 1 wherein said osteogenic protein is OP-1.

Claim 6 (withdrawn): The device of claim 1 wherein said device comprises at least two different osteogenic proteins.

Claim 7 (canceled).

Claim 8 (original): The device of claim 1 wherein said matrix is collagen.

Claim 9 (withdrawn): The device of claim 1 wherein said device comprises at least two different matrix materials.

Claim 10 (canceled).

Claim 11 (original): The device of claim 1 wherein said binding agent is selected from the group consisting of alkylcelluloses.

Claim 12 (original): The device of claim 1 wherein said binding agent is selected from the group consisting of methylcellulose, methylhydroxyethylcellulose, hydroxyethylcellulose, hydroxypropylmethylcellulose,

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carboxymethylcellulose, sodium carboxymethylcellulose, hydroxyalkylcelluloses, and admixtures thereof.

Claim 13 (original): The device of claim 1 wherein said binding agent is carboxymethylcellulose or the sodium salt thereof.

Claim 14 (withdrawn): The device of claim 1 wherein said device comprises at least two different binding agents.

Claim 15 (original): The device of claim 1 further comprising a wetting agent.

Claim 16 (original): The device of claim 15 wherein said wetting agent is saline.

Claim 17 (currently amended): A device for inducing local bone or cartilage formation, comprising at least approximately 1.25 mg of ~~purified~~ OP-1 and at least approximately 180 mg of carboxymethylcellulose per 1000 mg of collagen matrix, wherein ~~said purified OP-1 is isolated from naturally occurring sources or produced by recombinant DNA techniques, and~~ said carboxymethylcellulose has a viscosity of about 10-200 cP ~~or and~~ a degree of substitution of 0.65-0.90.

Claim 18 (previously presented): The device of claim 17 comprising at least approximately 2.5 mg of OP-1 per 1000 mg of collagen matrix.

Claim 19 (previously presented): The device of claim 17 or 18 comprising at least approximately 200 mg of carboxymethylcellulose per 1000 mg of collagen matrix.

Claim 20 (currently amended): The device of claim 1
wherein the binding agent to matrix ratio is ~~A device for~~
~~inducing local cartilage or bone formation comprising a~~
~~purified osteogenic protein capable of inducing repair of~~
~~endochondral bone, or cartilage, chondral, or osteochondral~~
~~defects and a carrier, wherein said carrier comprises one part~~
~~by weight binding agent to and 1-10 or fewer parts by weight~~
~~(w/w) matrix, said purified osteogenic protein is isolated~~
~~from naturally occurring sources or produced by recombinant~~
~~DNA techniques, and said binding agent has a viscosity of~~
~~about 10-200 cP or a degree of substitution of 0.65-0.90.~~

Claim 21 (currently amended): The device of claim 20
wherein said carrier comprises the binding agent to matrix
ratio is one part by weight binding agent to and 5 parts by
weight (w/w) matrix.

Claim 22 (currently amended): The device of claim 20 wherein ~~said carrier comprises the binding agent to matrix ratio is one part by weight binding agent to fewer than 1-5 parts by weight (w/w) matrix.~~

Claim 23 (currently amended): The device of claim 1 ~~A device for inducing local bone or cartilage formation comprising a purified osteogenic protein capable of inducing repair of endochondral bone, or cartilage, chondral, or osteochondral defects and a carrier, wherein said carrier comprises the binding agent to matrix ratio is 1-10 or fewer parts by weight (w/w) binding agent to and 1 part by weight matrix, said purified osteogenic protein being isolated from naturally occurring sources or produced by recombinant DNA techniques, and said binding agent has a viscosity of about 10-200 cP or a degree of substitution of 0.65-0.90.~~

Claim 24 (currently amended): The device of claim 23 wherein ~~said carrier comprises the binding agent to matrix ratio is fewer than 10 parts by weight (w/w) binding agent to one part by weight matrix.~~

Claim 25 (original): The device of claim 17, 18 or 19 further comprising saline.

Claims 26-30 (canceled).

Claim 31 (currently amended): A device for inducing local bone or cartilage formation comprising:

~~purified OP-1;~~

collagen matrix; and

carboxymethylcellulose;

~~wherein said purified OP-1 is isolated from naturally occurring sources or produced by recombinant DNA techniques, and said carboxymethylcellulose has having a viscosity of about 10-200 cP or and a degree of substitution of 0.65-0.90.~~

Claim 32 (currently amended): A kit for inducing local bone or cartilage formation ~~using the device of claim 1~~, the kit comprising:

(a) a first receptacle adapted to house an the osteogenic protein and a non-synthetic, non-polymeric the matrix material selected from the group consisting of collagen, apatites, hydroxyapatites, tricalcium phosphates and admixtures thereof, and

(b) a second receptacle adapted to house a the binding agent selected from the group consisting of cellulose, and salts thereof,

~~wherein the osteogenic protein and matrix material are provided in the receptacle of part (a), and the binding agent is provided in the receptacle of part (b), and said binding agent has a viscosity of about 10-200 cP or and a degree of substitution of 0.65-0.90.~~

Claim 33 (previously presented): The kit of claim 32 further comprising a receptacle adapted to house a wetting agent.

Claim 34 (canceled).

Claim 35 (currently amended): A kit for inducing local bone or cartilage formation ~~using the device of claim 1,~~ the kit comprising:

a first receptacle adapted to house an the osteogenic protein, a non-synthetic, non-polymeric the matrix material selected from the group consisting of collagen, apatites, hydroxyapatites, tricalcium phosphates, and

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admixtures thereof, and a ~~the~~ binding agent selected from the
group consisting of cellulose, and salts thereof,

wherein ~~the osteogenic protein, matrix material and~~
~~binding agent are provided in said receptacle, and said~~
binding agent has a viscosity of about 10-200 cP ~~or and~~ a
degree of substitution of 0.65-0.90.

Claim 36 (previously presented): The kit of claim 35,
further comprising a second receptacle adapted to house a
wetting agent.